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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/645,706	08/24/2000	Keith V. Wood	341.005US1	3329

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
02/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/645,706	WOOD ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 9, 11, 12, 15, 18, 20, 21, 24-39, 41-45, 47, 60,, 67, 69-71, 74, 76-78, 80-82, 86-88, 90, and 92-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/08, 1/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,3-5,9,11,12,15,18,20,21,24-39,41-45,47,60,64,67,69-71,74,76-78,80-82,86-88,90 and 92-96.

A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 11/6/08 has been entered.

Claims 2, 6-8, 10, 13, 14, 16, 17, 19, 22, 23, 40, 46, 48-59, 61-63, 65-66, 68, 72-73, 75, 79, 83-85, 89, and 91 have been canceled. Claims 1, 3-5, 9, 11, 12, 15, 18, 20, 21, 24-39, 41-45, 47, 60, 64, 67, 69-71, 74, 76-78, 80-82, 86-88, 90, and 92-96 are at issue and are present for examination. Claim 64 remains withdrawn as drawn to a non-elected invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly

owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 9, 11, 12, 15, 20, 21, 24-39, 41-45, 60, 67, 69, 70, 81, 86 and 90, and 92-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherf et al. (US Patent 5,670,356) in view of Zolotukhin et al. (US Patent 5,874,304), Donnelly et al. (WO 97/47358), Pan et al., Cornelissen et al. (US Patent 5,952,547), and Hey et al. (US Patent 6,169,232).

Sherf et al. teach a modified firefly luciferase gene in which 14% of the codons have been altered without altering the protein coding sequence such that the altered sequences were designed to optimize the codon selection for human host cells and eliminate restriction sites and sequences which encode transcription factor binding sites for known mammalian transcription factors including ATF, AP1, Sp1, AP2 etc. which would interfere with its genetically neutral behavior expected of a reporter gene. The altered gene includes at least 6 fewer transcription factor binding sites and was inserted into several mammalian expression vectors. The altered gene is transcribed and translated efficiently in mammalian host cells. The altered luciferase differs from the variant nucleic acids of the claims

in that 25% or more of the codons were not altered. Sherf et al. further disclose that similar modifications could be made to other luciferase genes including click beetle luciferase genes.

Zolotukhin et al. teach a modified *Aequorea victoria* GFP gene in which 37% of the codons have been altered (and optionally up to even 80-90% may be altered) without altering the protein coding sequence such that the altered sequences were designed to optimize the codon selection for human host cells. The optimized gene is inserted into an expression vector including a Kozak consensus sequence preceding the ATG initiation codon which optionally may include a multiple cloning site positioned between the promoter and the humanized GFP gene and/or downstream of the GFP gene. The altered gene preferably includes CTG codons encoding leucine, GTG or GTC codons encoding valine, GGC codons encoding glycine, ATC codons encoding isoleucine, CCT codons encoding proline, CGC codons encoding arginine, AGC codons encoding serine, ACC codons encoding threonine, and GGC or GGT codons encoding alanine and is transcribed and translated 5-10 times more efficiently in human cells than the wild type gene.

Donnelly et al. teach a modified hepatitis C virus core antigen gene in which 61% of the codons have been altered without altering the protein coding sequence such that the

altered sequences were designed to optimize the codon selection for human host cells and eliminate sequences which encode undesired sequences (such as ATTTA sequences, intron splice sites, etc.) generated by the alteration of the natural codons (see pages 17-18).

Pan et al. teach a modified *Plasmodium falciparum* gene in which a large number of the codons have been altered without altering the protein coding sequence such that the altered sequences were designed to optimize the codon selection for human host cells and eliminate sequences which might be detrimental to transcription and translation of the synthetic gene including sequences of promoters, poly A signals, intron splice sites and long runs of purines which might act as transcriptional termination sequences (see pages 1095). It should be noted that the elimination of undesired sequences was performed after the modification of the codon preference and thus would eliminate undesired sequences artificially introduced by the change in codons. The modified gene was successfully expressed in a variety of host cells (see page 1096) while expression of the unmodified gene has turned out to be difficult if not impossible (see page 1095).

Cornelissen et al. teach a modified *Bacillus thuringiensis* gene in which a small number of the codons have been altered

without altering the protein coding sequence such that the altered sequences were designed to eliminate sequences which might be detrimental to transcription and translation of the synthetic gene and particularly to eliminate sequences of cryptic promoters or DNA regulatory elements thereof which specifically interact with nuclear proteins (i.e., transcription factor binding sequences), see column 5, line 55 - column 6, line 15), and intron splice sites. The modified gene was successfully expressed in transgenic plants.

Hey et al. teach a plant sink protein gene in which a large number of the codons have been altered without altering the protein coding sequence such that the altered sequences were designed to optimize the codon selection for plant host cells and eliminate sequences which might be detrimental to transcription and translation of the synthetic gene including sequences of promoters, or elements thereof such as TATA box regions (i.e., a transcription factor binding sequence), poly A signals, intron splice sites, transcriptional termination sequences and runs of 4 or more pyrimidines which might interfere with transcription (see columns 9-12). It should be noted that the elimination of undesired sequences was performed after the modification of the codon preference and thus would

eliminate undesired sequences artificially introduced by the change in codons.

Therefore, it would have been obvious to further modify the luciferase gene of Sherf et al. to both increase the codon preference for humans as each of Zolotukhin et al., Donnelly et al., Pan et al. and Hey et al. each teach modifying a large percentage of the codons of a gene to be expressed in a host of interest and to remove potential promoter sequences, transcription binding factor sites, polyadenylation sites and splice sites as each of Sherf et al., Donnelly et al., Pan et al., Cornelissen et al. and Hey et al. each teach modifying at least several codons of a gene to be expressed in a desired host cell to match the codon preference of the host cell and/or to eliminate undesired sequences in order to increase its expression in the desired host cell and therefore increase its usefulness as a reporter gene in human and other desired host cells. One would have had a reasonable expectation of success in view of the results of the cited references which show that such alterations of other genes substantially improve the levels of expression in a desired host.

Applicants argue that while generally an artisan in view of the cited references would likely prepare synthetic nucleic acids which are optimized in some manner each reference

optimizes a gene in a different way. This argument presumably is intended to imply that while optimization in general is obvious optimization as claimed by applicants is not although applicants do not explicitly state this. However, this is NOT persuasive because applicants claims DO NOT in fact limit themselves to optimization of specific genes by specific changes as applicants imply. Instead applicants claims include any of an infinitely large number of changes of particular types (from which any combination of these types of changes which include reducing the number of transcription factor binding sites (TFBS) can be selected) to any of an enormous number of possible parent nucleic acids. As such applicants claims are reciting an enormous genera of nucleic acids prepared by methods that are obvious over the art as described. Applicants are merely reiterating repeatedly their arguments made in their Appeal Brief and rejected by the Board previously. As stated by the BPAI in their Decision:

> "Appellants argue that "the problem in the art (improved expression of genes in heterologous systems) has been 'solved' by each of the cited documents (in different ways) and so one of skill in the art would not look to combining the references in a particular way in the absence of Appellant's disclosure" (App. Br. 38). In *KSR*, the Supreme Court indicated that "[w]hen a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its

> patentability." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007). The evidence of record (FF 16-26) demonstrates that Appellants combination is a predictable application of the prior art methods to remove unwanted sequences which interfere with expression."

Applicants argue that the examiners previous statements that 1) it is obvious on its face that anytime a gene sequence is altered that one necessarily creates new sequences which were not previously present and that merely by random chance some of these newly created sequences may be detrimental and it is even further obvious on its face that the more changes one makes, the higher the chances that such a detrimental sequence will be introduced and 2) the remaining art clearly would have motivated one of skill in the art to make more substantial changes in codon preference within the luciferase of Sherf et al. are contradictory and questions why would one make more changes when more changes would just increase the chances that a detrimental sequence would be introduced. However, this is not persuasive because the art clearly suggests that one will obtain greater increases in expression with higher levels of optimization. While this clearly increases the chances that a detrimental sequence will be **introduced**, the art also teaches how to remedy this potential drawback by rechecking the optimized sequence to eliminate newly created undesired sequences. Therefore, this potential drawback would not have prevented a skilled artisan

from making more substantial changes in codon preference within the luciferase of Sherf et al. This argument was also made in applicants previous Brief and not found persuasive by the BPAI.

Applicants argue that while it is relatively straightforward to remove ATTTA sequences, splice sites, restriction enzyme sites, prokaryotic promoter sequences, po1y(A) signals, RNA polymerase termination signals, inverted repeats, long runs of purines, TA and CG doublets, and blocks of G or C residues of more than about 4 residues, to remove a plurality of transcription factor binding sites, by replacing codons, the modifications must be selected in context, i.e., with reference to how those modifications impact adjacent sequences. However, this is not persuasive because while removing transcription factor binding sites might require more than a single nucleotide change to accomplish and might be more difficult than removing other sites, there is no reason to believe (and applicants do not present one) that a skilled artisan could not select alterations to the sequence which would eliminate these sites as well even if this required modifying more than one nucleotide of the sequence. Clearly Sherf et al. managed to eliminate several TFBS in the wild type luciferase gene successfully. This argument was also made in applicants previous Brief and not found persuasive by the BPAI.

Applicants argue that Sherf et al. disclose that the improved reporter activity is due to the inactivation of the peroxisomal targeting sequence and not to structural nuances of the modifications and other modifications of the luciferases revealed that eliminating a palindrome sequence...also yielded greater expression. Thus, apparently modifications other than inactivation of the peroxisomal targeting sequence and elimination of palindromic sequences had little if any effect on reporter expression. Therefore, Sherf et al. teach away from modifications that include TFBS to improve reporter activity. However, this is not persuasive because this teaching does NOT in fact teach away for the instant invention. While in the case of Sherf et al. the largest increases in expression of the gene may have in fact resulted from the removal of the peroxisomal targeting sequence and not from the other changes, Sherf et al. clearly still teaches making the other types of changes, the other art cited in the rejection clearly do suggest that other changes do provide for increased expression of such genes and Sherf et al. identify additional reasons (i.e., sequences which encode transcription factor binding sites for mammalian transcription factors would interfere with the genetically neutral behavior expected of a reporter gene) which would motivate one to remove TFBS from an optimized reporter gene even

if they had no expectation that increased expression would result therefrom.

Applicants argue that their invention is not the simple substitution of one of the types of sites disclosed in, for example, Pan et al. for alteration of the msp-1 gene, with the TFBS disclosed in Sherf et al. for alteration of the luc gene, or the mere application of identifying undesirable sites in a nucleic acid sequence for removal. There is nothing in the cited art that discloses the large number of mammalian TFBS that are present in a mammalian codon optimized reporter protein encoding sequence. Because higher usage codons are those employed more frequently in a particular organism and nucleic acid sequences likely evolved to not include spurious TFBS but to include generally higher usage codons, it was unexpected that introducing mammalian codons, or replacing mammalian high usage codons with other mammalian codons, introduced mammalian TFBS. However, this is not persuasive. Applicants statement as to what their invention is not is noted but while they state what they think their invention is not they don't in fact state what their invention is and how that differs from what is obvious for the instantly cited references. As has been stated repeatedly, applicants invention is NOT limited to specific changes of specific genes. Furthermore, applicants argument that it was

unexpected that introducing mammalian codons, or replacing mammalian high usage codons with other mammalian codons, introduced mammalian TFBS is completely incorrect as it is obvious on its face that anytime a gene sequence is altered that one necessarily creates new sequences which were not previously present (and therefore not already subjected to optimization by natural selection) and that merely by random chance some of these newly created sequences may be detrimental and it is even further obvious on its face that the more changes one makes, the higher the chances that such a detrimental sequence will be introduced.

Claims 18, 47, 71, 74, 76-78, 80, 82, 87, 88 and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherf et al. (US Patent 5,670,356) in view of Zolotukhin et al. (US Patent 5,874,304), Donnelly et al. (WO 97/47358), Pan et al., Cornelissen et al. (US Patent 5,952,547), and Hey et al. (US Patent 6,169,232) as applied to claims 1, 3-5, 9, 11, 12, 15, 20, 21, 24-39, 41-45, 60, 67, 69, 70, 81, 86 and 90, and 92-95 above, and further in of Wood et al. (WO 99/14336).

Sherf et al., Zolotukhin et al., Donnelly et al., Pan et al., Cornelissen et al., and Hey et al. are discussed above. Sherf et al. teach that additional genes encoding luciferase can be similarly optimized for human expression. Wood et al. teach a

gene encoding a yellow green click beetle luciferase gene (wild-type Luc*Ppl*YG) having 100% identity to SEQ ID NO:23 and 97% identity to the protein encoded by SEQ ID NO:2 herein. Therefore, it would have been obvious to one of skill in the art to optimize the expression of the yellow-green click beetle luciferase gene of Wood et al. in human cells as taught by the combined disclosures of Sherf et al., Zolotukhin et al., Donnelly et al., Pan et al., Cornelissen et al., and Hey et al.

Applicants only argument specific to the instant rejection is that one of skill in the art could not prepare synthetic nucleic acids which hybridize to the SEQ ID numbers recited in claim 18 without preparing the recited SEQ ID numbers. However, this is completely untrue. In fact it is noted that applicants made the recited nucleic acids (i.e., SEQ ID NOs:7-9 and 297) by altering a different nucleic acid. One could prepare a nucleic acid within the scope of these claims by many different methods including direct synthesis or by altering a different parent nucleic acid which encodes a protein similar or identical to SEQ ID NO:23 (such as the nucleic acid of Wood et al.) by codon optimization and removal of unwanted sequences created by the optimization as taught by the cited references. Following the suggestions of Zolotukhin et al. with regard to specific codon optimization choices for high level expression in human

cells followed by modifications to eliminate undesirable sequences as taught by the secondary references, while not leading a skilled artisan to the specific nucleotide sequence of SEQ ID NO:9, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:18, SEQ ID NO:297, or SEQ ID NO:301 (as this would require that the art suggest all of applicants specific modification choices) would lead a skilled artisan to produce a optimized sequence which would hybridize to SEQ ID NO:9 under high stringency conditions as high stringency hybridization conditions still allow for a substantial number of positions (i.e., up to approximately 5% of the total; i.e., approximately 81 nucleotides in this case) in which the individual choices could be different. In fact it is noted that applicants made the recited nucleic acids (i.e., SEQ ID NOs:7-9, 18, 297, and 301 by altering a different

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5, 9, 11, 12, 15, 20, 21, 24-39, 41-45, 60, 67, 69, 70, 81, 86, 88, 90, and 92-95 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25-50 of copending Application No. 11/825,304. Claims 1, 3-5, 9, 11, 12, 15, 20, 21, 24-39, 41-45, 60, 67, 69, 70, 81, 86, 88, 90, and 92-95 herein and claims 25-50 of copending Application No. 11/825,304 are all directed to synthetic nucleic acids encoding a firefly luciferase polypeptide in which many of the codons have been replaced with mammalian high usage codons or codons selected to reduce the number of transcription factor binding sequences present in a wild-type sequence or introduced by the codon optimization. The claims differ in a variety of individual features such as the wild type nucleic acid modified and the number of alterations of the sequence of the wild-type gene polypeptide which may be introduced into the polypeptide encoded

by the synthetic nucleic acid. However the preferred embodiments of the synthetic nucleic acid molecules of the copending application would clearly anticipate claims 1, 3-5, 9, 11, 12, 15, 20, 21, 24-39, 41-45, 60, 67, 69, 70, 81, 86, 88, 90, and 92-95 herein. Claims 1, 3-5, 9, 11, 12, 15, 20, 21, 24-39, 41-45, 60, 67, 69, 70, 81, 86, 88, 90, and 92-95 herein cannot be considered patentably distinct over claims 25-50 of copending Application No. 11/825,304 when there is a specifically recited embodiment that would anticipate the instant claims. Alternatively, claims 1, 3-5, 9, 11, 12, 15, 20, 21, 24-39, 41-45, 60, 67, 69, 70, 81, 86, 88, 90, and 92-95 herein cannot be considered patentably distinct over claims 25-50 of copending Application No. 11/825,304 when there is a specifically disclosed embodiment in the copending application that supports claims 25-50 of copending Application No. 11/825,304 and falls within the scope of claims 1, 3-5, 9, 11, 12, 15, 20, 21, 24-39, 41-45, 60, 67, 69, 70, 81, 86, 88, 90, and 92-95 herein because it would have been obvious to one having ordinary skill in the art to select the preferred embodiments of synthetic nucleic acids that support the claims of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3-5, 9, 11, 12, 15, 18, 20, 21, 24-39, 41-45, 47, 60, 67, 69-71, 74, 76-78, 80-82, 86-88, 90, and 92-96 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 8-13, 15, 17-21, 24-45, and 60-62 of copending Application No. 11/786,785. Claims 1, 3-5, 9, 11, 12, 15, 18, 20, 21, 24-39, 41-45, 47, 60, 67, 69-71, 74, 76-78, 80-82, 86-88, 90, and 92-96 herein and claims 1-5, 8-13, 15, 17-21, 24-45, and 60-62 of copending Application No. 11/786,785 are all directed to synthetic nucleic acids encoding a firefly luciferase polypeptide in which many of the codons have been replaced with mammalian high usage codons or codons selected to reduce the number of transcription factor binding sequences present in a wild-type sequence or introduced by the codon optimization. The claims differ in a variety of individual features such as the wild type nucleic acid modified and the number of alterations of the sequence of the wild-type gene polypeptide which may be introduced into the polypeptide encoded by the synthetic nucleic acid. However the preferred embodiments of the synthetic nucleic acid molecules of the

copending application would clearly anticipate claims 11, 3-5, 9, 11, 12, 15, 18, 20, 21, 24-39, 41-45, 47, 60, 67, 69-71, 74, 76-78, 80-82, 86-88, 90, and 92-96 herein. Claims 1, 3-5, 9, 11, 12, 15, 18, 20, 21, 24-39, 41-45, 47, 60, 67, 69-71, 74, 76-78, 80-82, 86-88, 90, and 92-96 herein cannot be considered patentably distinct over claims 1-5, 8-13, 15, 17-21, 24-45, and 60-62 of copending Application No. 11/786,785 when there is a specifically recited embodiment that would anticipate the instant claims. Alternatively, claims 1, 3-5, 9, 11, 12, 15, 18, 20, 21, 24-39, 41-45, 47, 60, 67, 69-71, 74, 76-78, 80-82, 86-88, 90, and 92-96 herein cannot be considered patentably distinct over claims 1-5, 8-13, 15, 17-21, 24-45, and 60-62 of copending Application No. 11/786,785 when there is a specifically disclosed embodiment in the copending application that supports claims 1-5, 8-13, 15, 17-21, 24-45, and 60-62 of copending Application No. 11/786,785 and falls within the scope of claims 1, 3-5, 9, 11, 12, 15, 18, 20, 21, 24-39, 41-45, 47, 60, 67, 69-71, 74, 76-78, 80-82, 86-88, 90, and 92-96 herein because it would have been obvious to one having ordinary skill in the art to select the preferred embodiments of synthetic nucleic acids that support the claims of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The references lined through on applicants IDS file 11/06/08 were lined through because they were duplicates of other citations on the same IDS or because the references cited were not submitted.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). Applicant should note that while the provisional ODP rejections of the claims were not previously presented, these rejections are only provisional rejections, were the result of applicants actions following the previous final rejection and the instant application could be allowed without a terminal disclaimer despite these rejections and thus the finality of the instant office action is considered proper

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed, can be reached at (571) 272-0934. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
Art Unit 1652